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# Meeting the Challenge of the Methamphetamine Crisis

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*VISN 20 MIRECC Presents  
February 2<sup>nd</sup>, 2022*

*Dominick DePhilippis, Ph.D.*

*VA Deputy National Mental Health Director, Substance Use Disorder  
VA Office of Mental Health and Suicide Prevention*

# Objectives

The participant will be able to:

- 1) Describe the scope of the methamphetamine crisis
- 2) Identify effective, evidence-based treatments for stimulant use disorder
- 3) Distinguish the behavioral principles upon which effective CM practice is based

# THE CHALLENGE OF RECOVERY FROM SUD

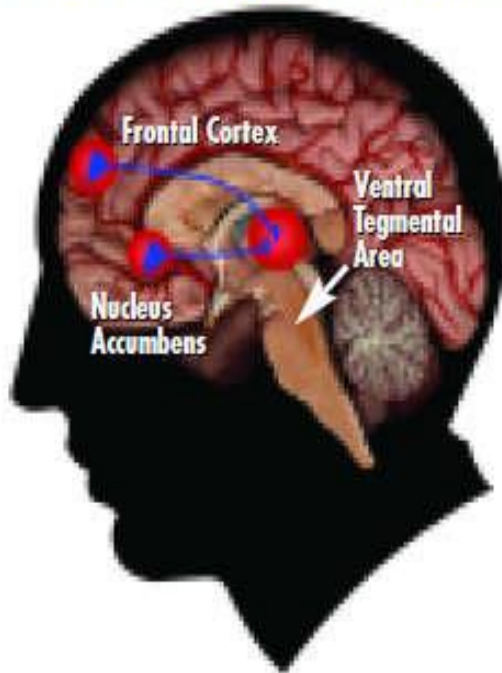
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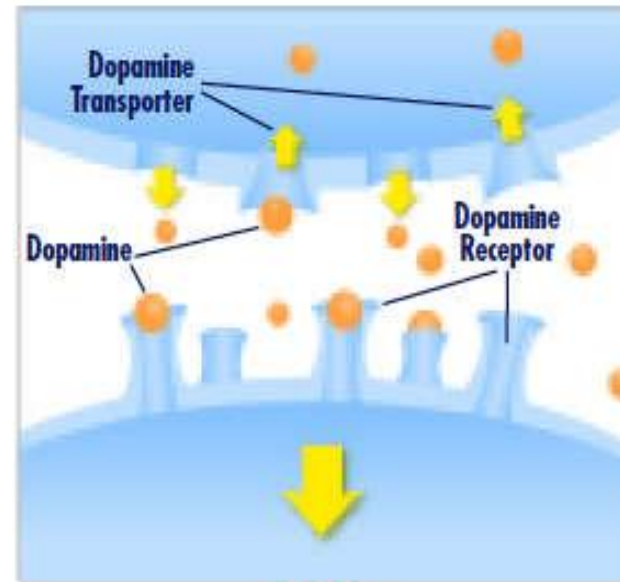
# Recovery from SUD: The Neurophysiological Challenge

## Brain reward (dopamine) pathways

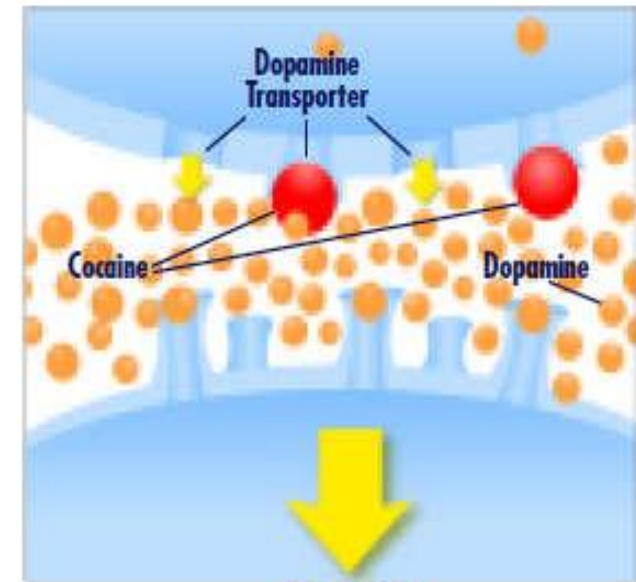


These brain circuits are important for natural rewards such as food, music, and sex.

## Drugs of abuse increase dopamine



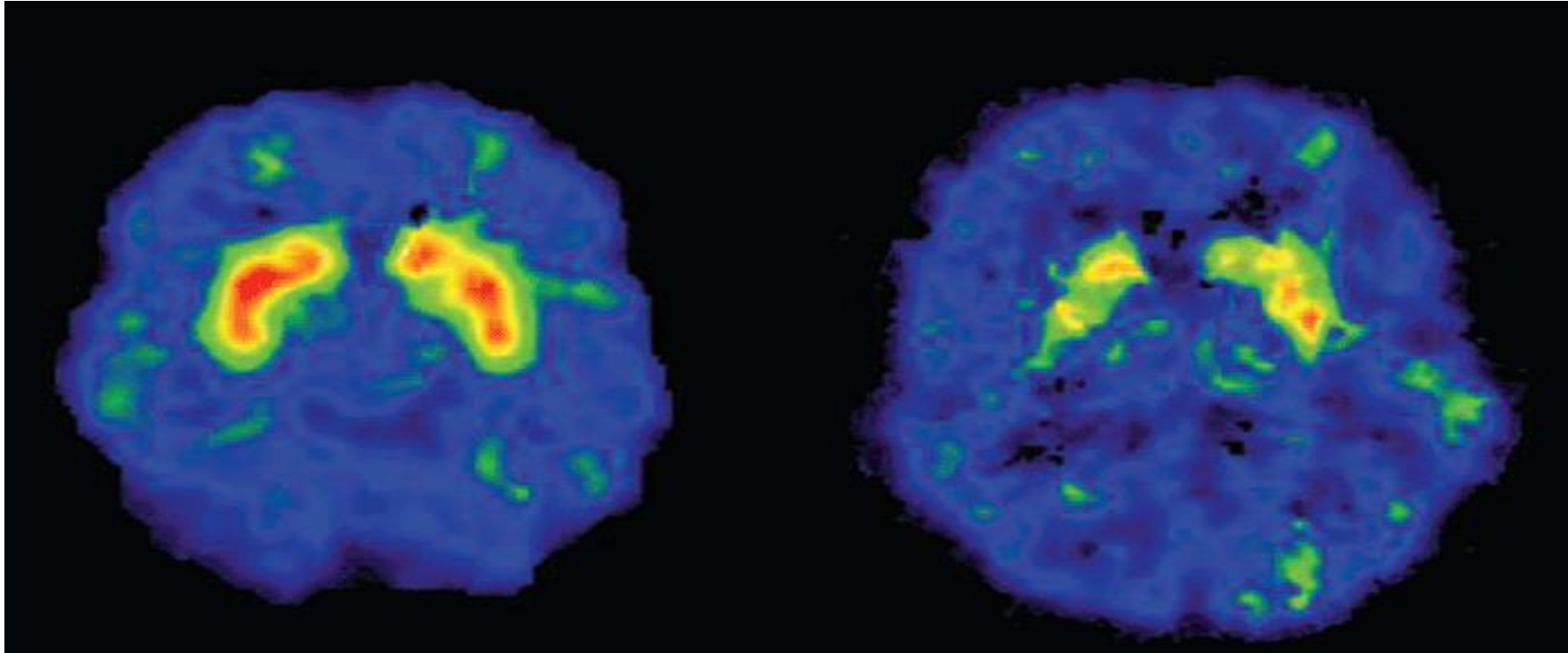
**FOOD**



**COCAINE**

Typically, dopamine increases in response to natural rewards such as food. When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

# Recovery from SUD: The Neurophysiological Challenge



Healthy Control

Stimulant Use Disorder

<https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain>

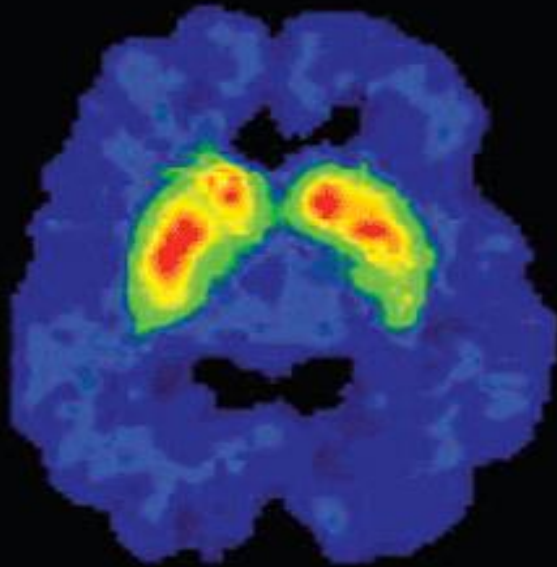
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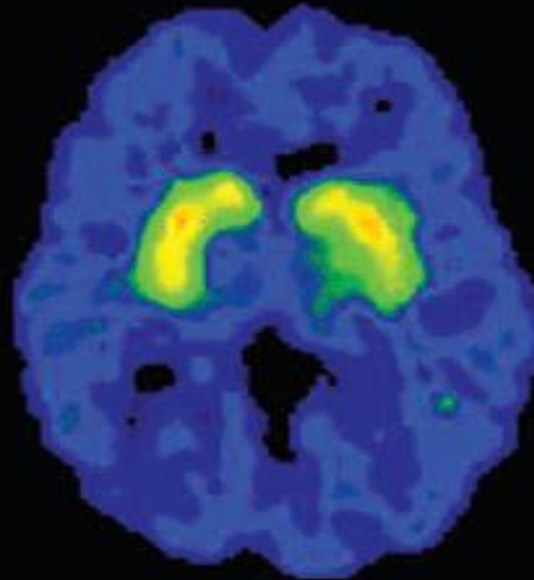
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# Recovery from SUD: The Time Challenge

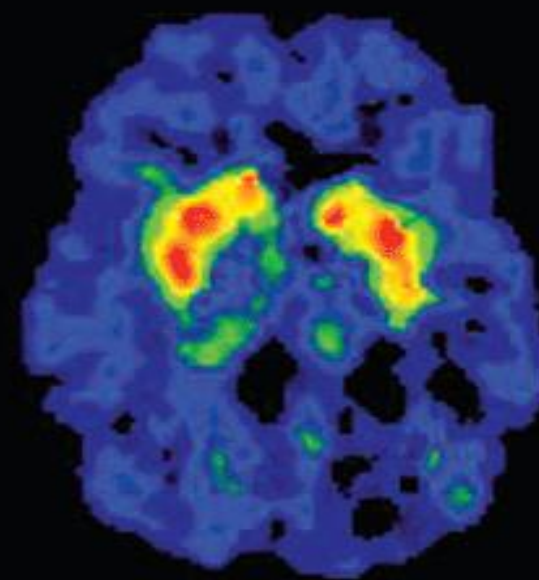
BRAIN RECOVERY WITH PROLONGED ABSTINENCE



Healthy Control



One month  
abstinent from  
Methamphetamine



14 months  
abstinent from  
Methamphetamine

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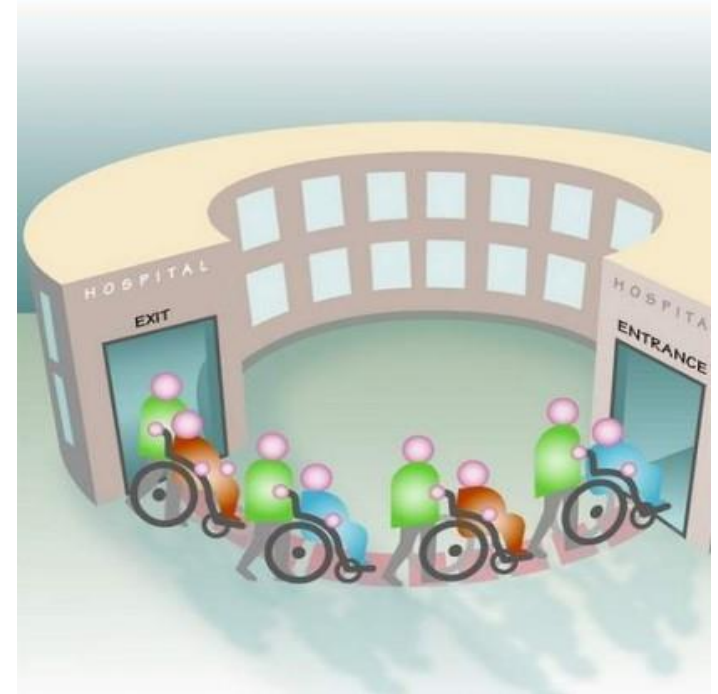


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# Recovery from SUD: The Treatment Attrition Challenge

- SUDs are chronic illnesses that respond best to continuing care. Yet traditional treatment attendance is often sporadic.
- Attrition rates range from 50% to 60% among inpatients to more than 70% after just four sessions of outpatient treatment.
- Repeated (rather than continuous) episodes of SUD specialty care are associated with greater subsequent utilization of high cost services (Hawkins et al., *JSAT*, 2012).



# Recovery from SUD: The Cognitive-Behavioral Challenge

- Patients with SUDs face a daunting challenge:
  - On the one hand, substance use presents an opportunity for immediate positive and negative reinforcement and, typically, delayed and uncertain aversive (punitive) consequences.
  - On the other hand, recovery presents the opportunity for delayed and uncertain positive and negative reinforcement and, sometimes, immediate aversive (punitive) consequences, e.g. withdrawal, loss of SUD social network, lucid assessment of the devastation brought on by SUD.
- **Because immediacy of reinforcement is crucial, the challenge is to make recovery immediately reinforcing.**





# **METHAMPHETAMINE USE DISORDER: AN EXEMPLAR OF THE SUD RECOVERY CHALLENGE**

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# What is Methamphetamine?

- A potent, highly addictive, schedule II, CNS stimulant. It's a dopamine reuptake inhibitor (like cocaine) and also increases the release of dopamine into the synapse.
- Derived from amphetamine, it's more potent and has longer-lasting effects (half-life is 12 hours vs. 1 hour for cocaine).
- Medicinally, it's sometimes used to treat ADHD, narcolepsy, and obesity.
- Most methamphetamine in the USA is produced by criminal organizations in Mexico. Sold relatively inexpensively and highly pure.
- Can be smoked, injected, snorted, or orally ingested. Latter two lead to euphoria; former two lead to a more intense but briefer "rush."
- Pattern of use often involves "binging and crashing" with lengthy binges referred to as "runs."



Crystal methamphetamine

Photo by

DEA/<https://www.dea.gov/galleries/drug-images/methamphetamine>

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# Effects of Methamphetamine: Immediate Reinforcement, Delayed Punishment

## Short-term effects may include:

- increased attention and decreased fatigue
- increased activity and wakefulness
- decreased appetite
- euphoria and rush
- increased respiration
- rapid/irregular heartbeat
- hyperthermia

## Long-term effects may include:

- addiction
- psychosis, including:
  - paranoia
  - hallucinations
  - repetitive motor activity
- changes in brain structure and function
- deficits in thinking and motor skills
- increased distractibility
- memory loss
- aggressive or violent behavior
- mood disturbances
- severe dental problems
- weight loss

**National Institute on Drug Abuse (NIDA)  
Methamphetamine**

Last Updated October 2019  
<https://www.drugabuse.gov>

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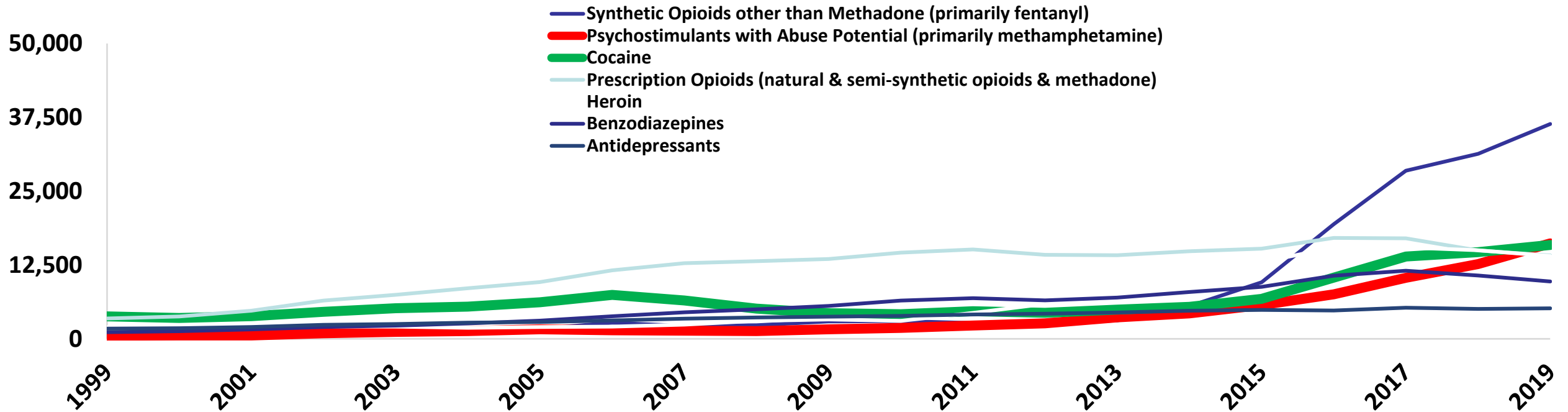


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# Stimulant Use Disorder: Scope of the Problem

- An estimated 1.1 million people aged >12 had methamphetamine use disorder in 2018, up from 684,000 in 2016. (*SAMHSA, 2019, NSDUH*)
- In 2018, 977,000 people aged >12 had a cocaine use disorder up from 867,000 in 2016. (*SAMHSA, 2019, NSDUH*)
- An estimated 561,000 people aged >12 had a prescription stimulant use disorder similar in the past year. (*SAMHSA, 2019, NSDUH*)
- Between 2012 to 2019, OD deaths involving cocaine increased 3-fold and those involving stimulants, including MA, increased 5-fold. (*Hedegaard et al., CDC, 2020*)
- Methamphetamine misuse cost the USA approximately \$23.4 billion in 2005 (*Nicosia et al., RAND Corp., 2009*).
- In some regions of the USA, it poses an even greater threat of fatal OD than opioids (*Hedegaard et al., CDC, 2019*).

# National Drug-Involved Overdose Deaths\*, Number Among All Ages, 1999-2019



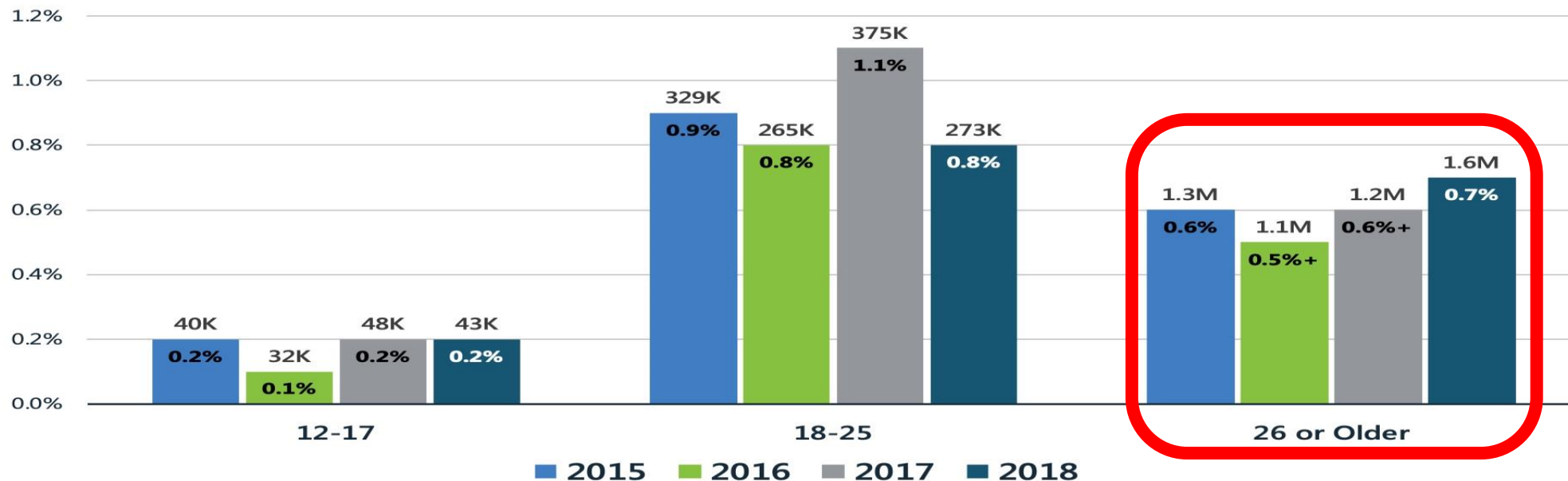
\*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2019 on CDC WONDER Online Database, released 12/2020.



# Methamphetamine (MA) Use: Significant Increase in Adults $\geq$ 26 y.o.

## Methamphetamine Use: Significant Increase in Adults $\geq$ 26 y.o.

PAST YEAR, 2015-2018 NSDUH, 12+



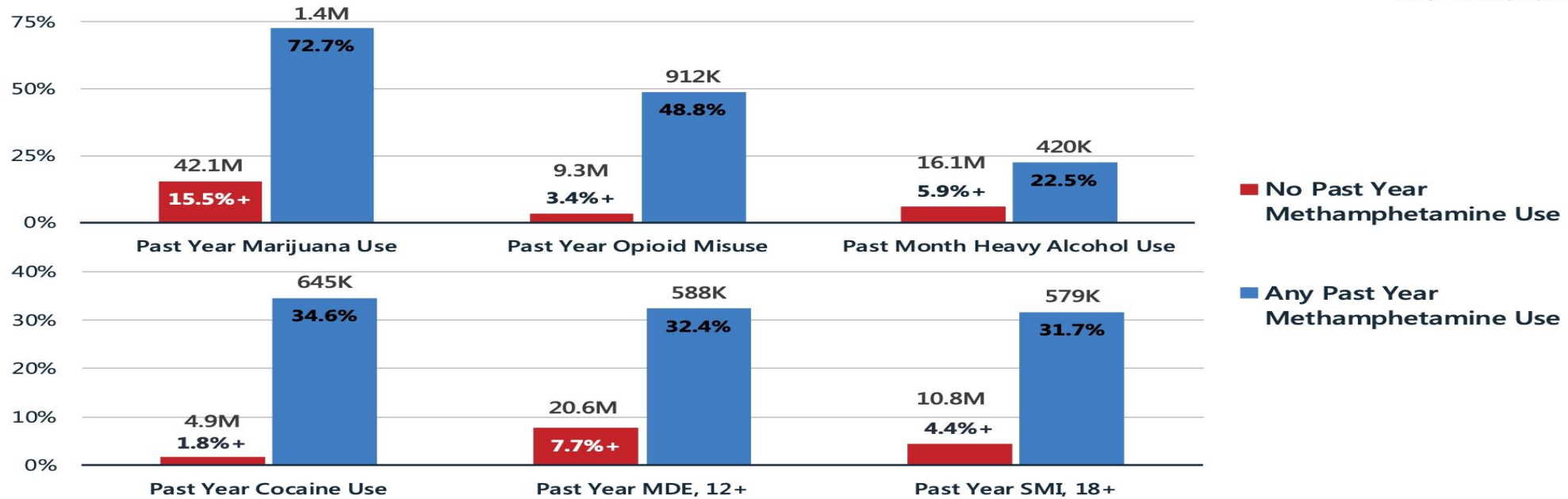
+ Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.

**SAMHSA**  
Substance Abuse and Mental Health  
Services Administration

# Methamphetamine Use Related to Other Substance Use, MDE, and SMI

## Methamphetamine Use Related to Other Substance Use, MDE and SMI

PAST YEAR/MONTH, 2018 NSDUH, 12+



+ Difference between this estimate and the estimate for people with past year methamphetamine use is statistically significant at the .05 level.

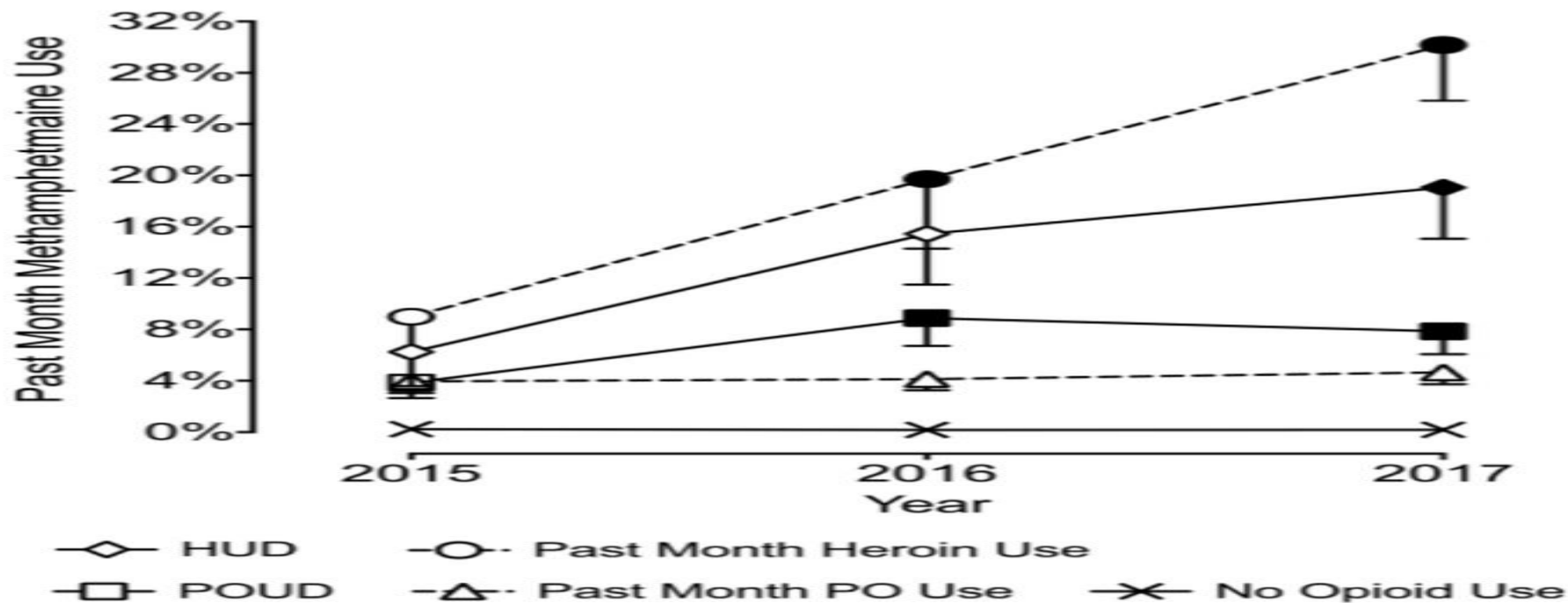


# Past Month MA Use by Opioid Use History

(Strickland et al., 2019, Drug Alcohol Depend., November 01; 204: 107592.)

Strickland et al.

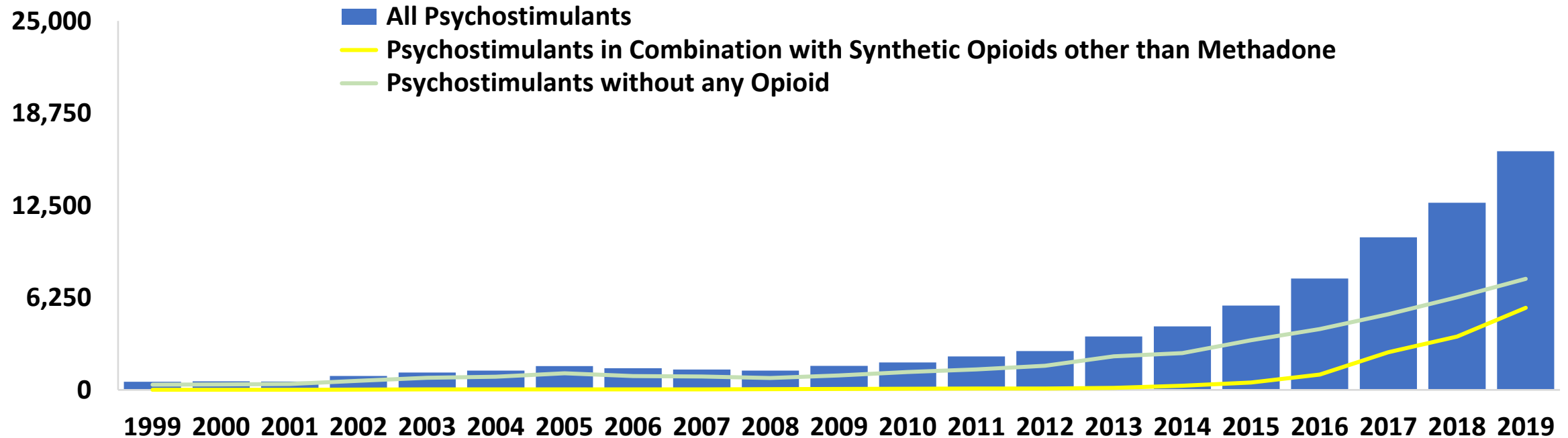
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**Figure 1.** Past Month Methamphetamine Use by Opioid Use History. Plotted are weighted prevalence estimates for past month methamphetamine use from the 2015-2017 NSDUH. Values are presented for past month heroin use (circles), past year heroin use disorder (diamonds), past month non-medical prescription opioid use (triangles), and past year non-medical prescription opioid use disorder (squares). Filled symbols are significantly different from 2015. Dotted lines represent substance use disorder variables and solid lines represent past month variables. Also plotted are estimates for individuals with no past month heroin or

Drug Alcohol Depend. Author manuscript; available in PMC 2020 November 01.

# National Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)\*, by Opioid Involvement, Number Among All Ages, 1999-2019



\*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above.

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2019 on CDC WONDER Online Database, released 12/2020.

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## Regional Differences in the Drugs Most Frequently Involved in Drug Overdose Deaths: United States, 2017

by Holly Hedegaard, M.D., M.S.P.H., and Brigham A. Bastian, B.S., National Center for Health Statistics; James P. Trinidad, M.P.H., M.S., U.S. Food and Drug Administration; and Merianne Rose Spencer, M.P.H., and Margaret Warner, Ph.D., National Center for Health Statistics

**Table A. Drugs most frequently involved in drug overdose deaths: United States, 2017**

Rank <sup>2</sup>	Referent drug group	United States (n = 70,237, 21.7) <sup>1</sup>		
		Number of deaths	Percent <sup>3</sup>	Age-adjusted rate <sup>4</sup>
1	Fentanyl .....	27,299	38.9	8.7
2	Heroin .....	15,982	22.8	5.0
3	Cocaine .....	14,948	21.3	4.6
4	Methamphetamine .....	9,356	13.3	2.9
5	Alprazolam .....	6,647	9.5	2.1
6	Oxycodone .....	6,053	8.6	1.8
7	Morphine .....	4,874	6.9	1.5
8	Methadone .....	3,286	4.7	1.0
9	Hydrocodone .....	3,072	4.4	0.9
10	Diphenhydramine .....	2,286	3.3	0.7
11	Clonazepam .....	2,055	2.9	0.6
12	Diazepam .....	2,025	2.9	0.6
13	Cabapentin .....	1,848	2.6	0.6
14	Amphetamine .....	1,581	2.3	0.5
15	Itramadol .....	1,333	1.9	0.4

<sup>1</sup>Number and age-adjusted rate (deaths per 100,000 standard population) for all drug overdose deaths. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 standard population.

<sup>2</sup>Drugs were ranked by number of deaths. Ranks were not tested for statistical significance.

<sup>3</sup>Percentage of drug overdose deaths that involve the referent drug group.

<sup>4</sup>Age-adjusted death rates (deaths per 100,000 standard population) were calculated using the direct method and adjusted to the 2000 standard population.

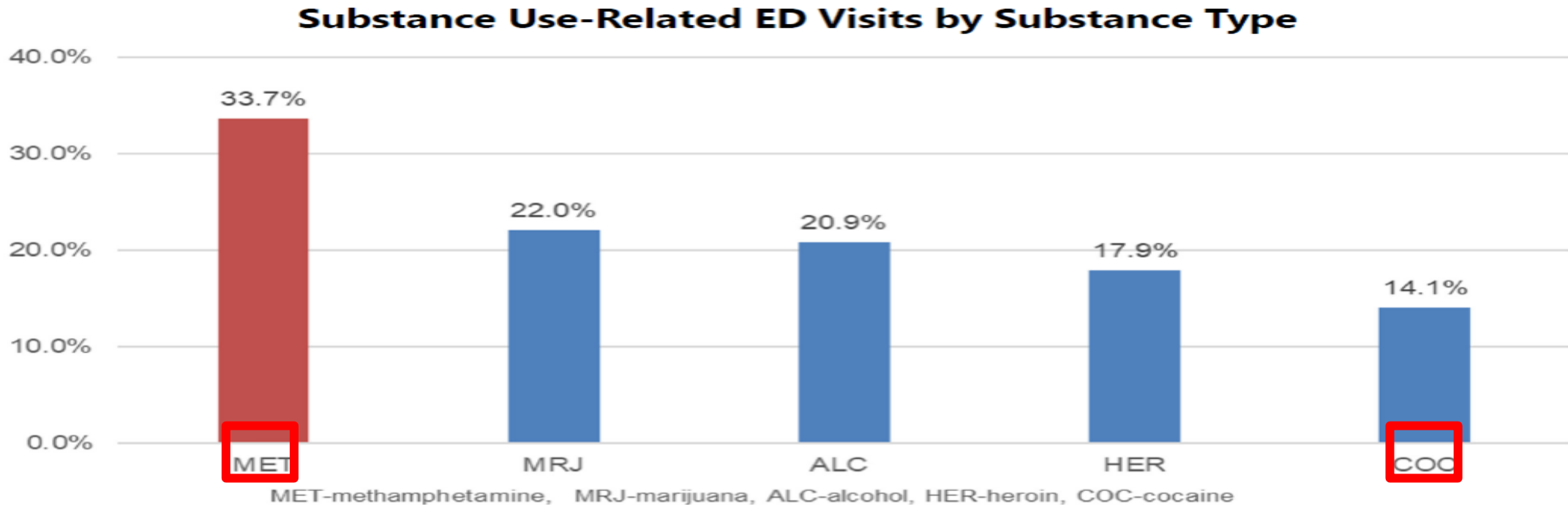
NOTES: Drug overdose deaths were identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent drug group. Deaths involving more than one referent drug group (e.g., a death involving both heroin and cocaine) were counted in both totals. To avoid counting the same death multiple times, the numbers for drug-specific deaths should not be summated.

SOURCE: NCHS National Vital Statistics System, Mortality files linked with death certificate literal text, 2017.



# 2020 Data from SAMHSA's Drug Abuse Warning Network (DAWN)

Data on substance-related ED visits from 50 non-Federal hospitals

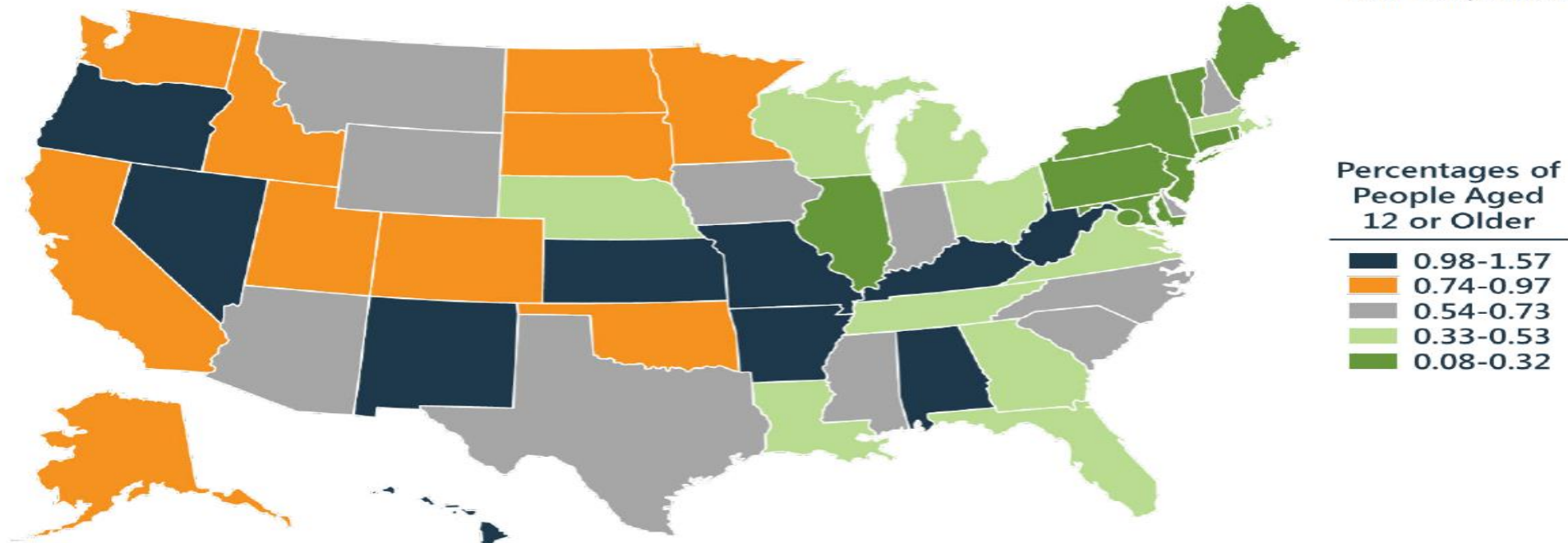


This graph shows substance use-related ED visits by substance type, focusing on the most common illicit substances and alcohol. Methamphetamine (33.7%) was the most common type of substance involved in substance use-related ED visits.

# Heat Map of Methamphetamine Use in the USA

## Methamphetamine Use by State

PAST YEAR, POOLED 2016-2017 NSDUH, 12+



Differences in colors across states do not indicate significant differences in estimates.

# SO, CAN STIMULANT USE DISORDER BE TREATED?

# Pharmacotherapy for methamphetamine/amphetamine use disorder—a systematic review and meta-analysis

Brian Chan<sup>1,2</sup>, Michele Freeman<sup>3</sup> , Karli Kondo<sup>3</sup>, Chelsea Ayers<sup>3</sup>, Jessica Montgomery<sup>3</sup>, Robin Paynter<sup>3</sup> & Devan Kansagara<sup>1,3,4</sup>

Division of General Internal Medicine and Geriatrics, Oregon Health and Science University, Portland, OR, USA,<sup>1</sup> Central City Concern, Portland, OR, USA,<sup>2</sup> Evidence-based Synthesis Program Center, VA Portland Health Care System, Portland, USA<sup>3</sup> and Department of Medicine, VA Portland Health Care System, Portland, OR, USA<sup>4</sup>

- There was low-strength evidence from two RCTs that methylphenidate may reduce MA/A use: 6.5 versus 2.8% MA/A-negative UDS in one study ( $n = 34$ ,  $P = 0.008$ ) and 23 versus 16% in another study ( $n = 54$ ,  $P = 0.047$ ).
- Antidepressants as a class had no statistically significant effect on abstinence or retention on the basis of moderate strength evidence.
- Studies of anticonvulsants, antipsychotics (aripiprazole), opioid antagonists (naltrexone), varenicline and atomoxetine provided either low-strength or insufficient evidence of no effect on the outcomes of interest.



# Pharmacological Treatment of Methamphetamine/Amphetamine Dependence: A Systematic Review

Krista J. Siefried<sup>1,2,3</sup> · Liam S. Acheson<sup>2</sup> · Nicholas Lintzeris<sup>4,5,6</sup> · Nadine Ezard<sup>1,2,3,6</sup>

Published online: 17 March 2020  
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- “No pharmacotherapy yielded convincing results for the treatment of AMPH/MA dependence; mostly studies were underpowered and had low treatment completion rates. However, there were positive signals from several agents that warrant further investigation in larger scale studies; agonist therapies show promise.”
- “Some studies demonstrated mixed or weak positive signals (often in defined populations, e.g. men who have sex with men), with some variation in efficacy signals dependent on baseline frequency of AMPH/MA use. The most consistent positive findings have been demonstrated with stimulant agonist treatment (dexamphetamine and methylphenidate), naltrexone and topiramate.”
- “Less consistent benefits have been shown with the antidepressants bupropion and mirtazapine, the glutamatergic agent riluzole and the corticotropin releasing factor (CRF-1) antagonist pexacerfont; whilst in general, antidepressant medications (e.g. selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants [TCAs]) have not been effective in reducing AMPH/MA use.”



# No FDA-Approved Pharmacotherapies & Insufficient Evidence to Recommend Any Pharmacotherapies

Per the 2021 VA-DoD Clinical Practice Guidelines for the treatment of Substance Use Disorders (SUD CPGs)...

***“There is insufficient evidence to recommend for or against the use of any pharmacotherapy for the treatment of cocaine use disorder or amphetamine/methamphetamine use disorder.”***

# TRIVEDI et al. (2021), *NEJM*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Bupropion and Naltrexone in Methamphetamine Use Disorder

M.H. Trivedi, R. Walker, W. Ling, A. dela Cruz, G. Sharma, T. Carmody, U.E. Ghitza, A. Wahle, M. Kim, K. Shores-Wilson, S. Sparenborg, P. Coffin, J. Schmitz, K. Wiest, G. Bart, S.C. Sonne, S. Wakhlu, A.J. Rush, E.V. Nunes, and S. Shoptaw

- 13.6% of the NTX-XR(380mg)–bupropion-XR(450mg) group vs. 2.5% of the placebo group had at least three methamphetamine negative urine samples out of four samples at the end of the 6-week trial (an overall treatment effect of 11.1 percentage points).
- The number needed to treat in order for one patient to have a response under the assumptions in this trial is 9.
- Adverse events included gastrointestinal disorders, tremor, malaise, hyperhidrosis, and anorexia. Serious adverse events occurred in 8 of 223 participants (3.6%) who received naltrexone–bupropion during the trial.

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# 2021 VA-DoD SUD CPGs: Psychosocial Treatments for Stimulant Use Disorder

- For patients with **cocaine use disorder**, we recommend one or more of the following interventions as initial treatment, considering patient preference and availability:
  - **Cognitive behavioral therapy**
  - Recovery-focused behavioral therapy (i.e., individual drug counseling and community reinforcement approach)
  - **Contingency management** in combination with another behavioral intervention considering patient preference and availability
- For patients with **amphetamine/methamphetamine use disorder**, we suggest offering **contingency management** as initial treatment in combination with another behavioral intervention, considering patient preference and availability.

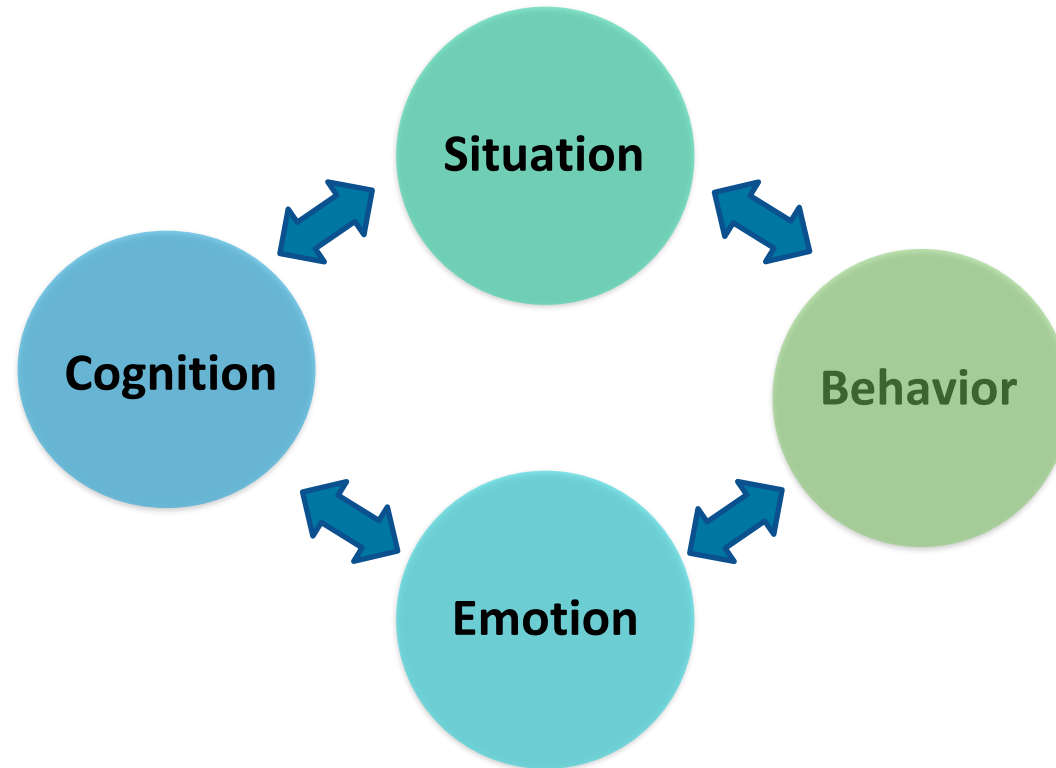
# THE FOUNDATIONS OF BEHAVIORAL TREATMENT OF STIMULANT USE DISORDER

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# The Organizing Principle of CBT-SUD: Reciprocal Determinism

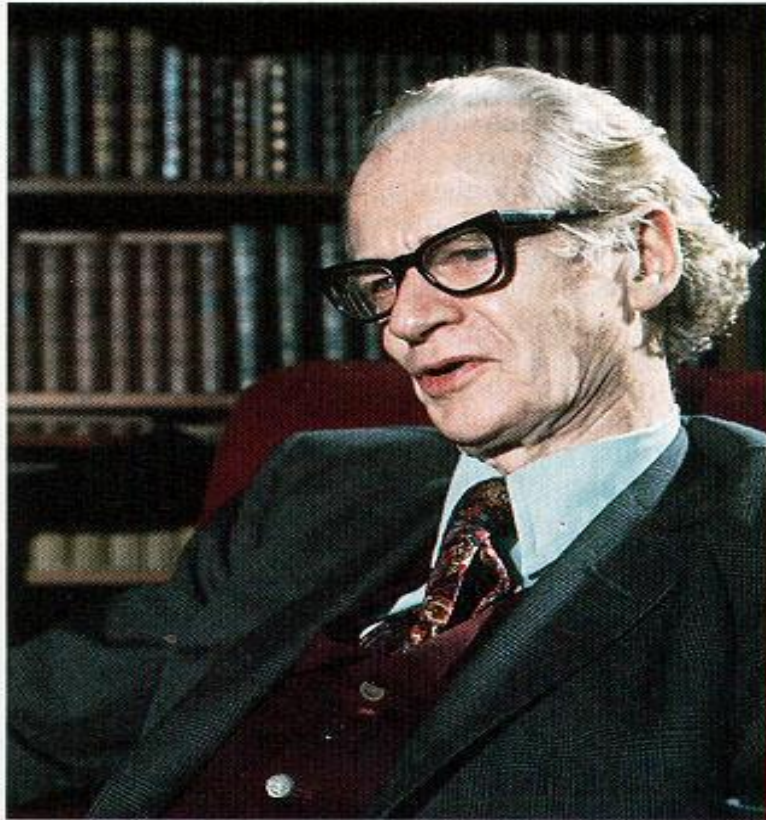




# The Organizing Principle of Contingency Management: Operant Conditioning (OC)

- Involves the acquisition of operant behavior: behavior that operates on the environment to produce stimuli (read: consequences).
- Began with the work of Edward Thorndike who formulated the Law of Effect => rewarded behavior is likely to recur.
- OC investigations continued with the work of B.F. Skinner and his use of the operant chamber (Skinner Box).

# B.F. Skinner and the Operant Chamber



1904-1990



# **Ok, So What Kinds of Consequences Follow Behavior?**

**Pleasant things**

**Unpleasant things**

**Nothing**

# Features of OC: Reinforcement

- Reinforcer: any event that increases the probability of recurrence of the behavior preceding it.
  - Positive Reinforcement: presentation of a pleasant consequence after a behavior occurs.
  - Negative Reinforcement: removing or reducing an unpleasant stimulus after a behavior occurs.

# Elements of OC: Extinction



- Extinction is the process of withholding reinforcement following a behavior.
- Because extinction affects the contingent association between the behavior and reinforcement, it makes behavior less likely to occur.
- In CM, extinction involves the withholding of reinforcement when the patient does not complete the target behavior, e.g. testing positive.

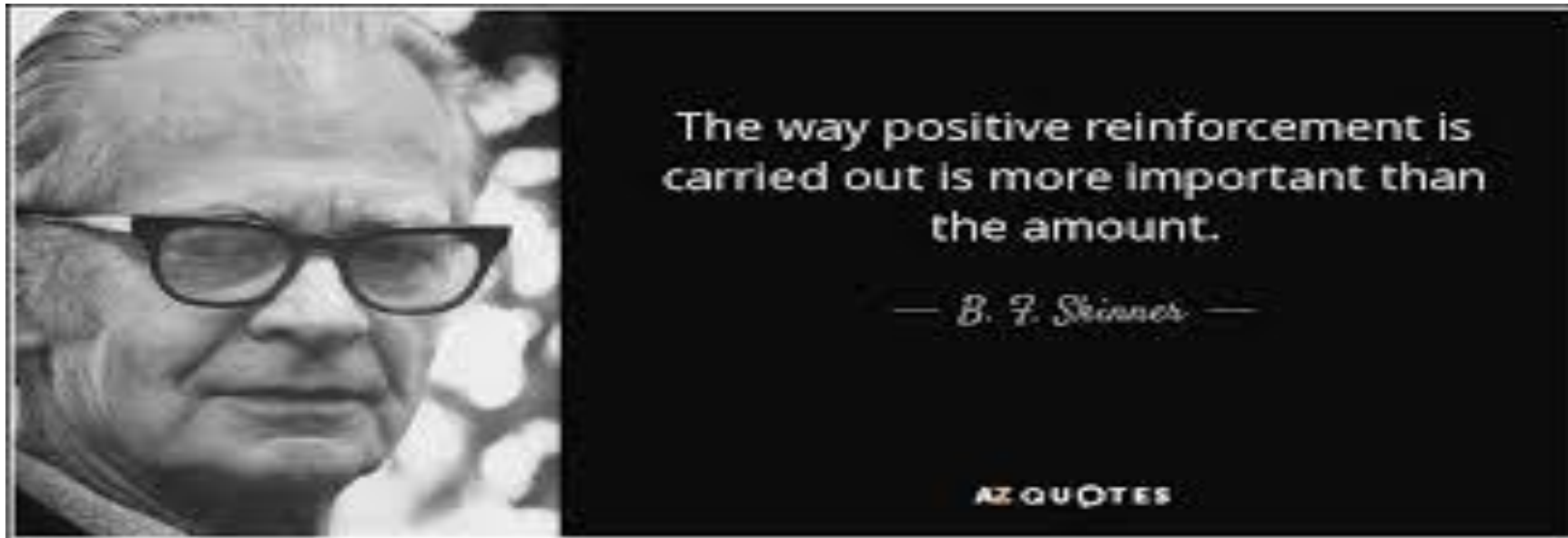




# That sounds easy enough...

## We reward patients for healthy behavior, right?

- Yes and No.
  - Yes, the concept is simple!
  - No, how one conducts CM makes all the difference in the world!



# The Prize CM Protocol

- Patients earn prizes of varying magnitude based on draws from a fishbowl.
- The fishbowl contains 500 prize slips:

250(50%) “Good Job!”	209(41.8%) “Small”=\$1
40 (8%) “Large”=\$20	1 (0.2%) “Jumbo”=\$100
- Draws start at 1 for the first negative sample and escalate (to a cap of ~8) with consistent abstinence.
- When abstinence is not verified, no draws are earned, and draws reset to 1 for the next negative sample.
- **Average cost per patient over 12 weeks is ~\$200.**

# **IMPLEMENTING CM: IS THE JUICE WORTH THE SQUEEZE?**

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# Abstinence CM Outcomes: The Empirical Literature

- Meta-analysis of 47 CM studies with treatment/control group design published between 1970-2002.
  - **Mean effect size =.42 (22% improvement in success rate).**
  - “Among the more effective approaches to promoting abstinence during the treatment of substance use disorders.”
    - **Prendergast et al., *Addiction*, 2006**
- Meta-analysis of 34 well-controlled studies of psychosocial SUD treatments (including CM, relapse prevention, CBT, and treatments combining CBT and CM) published between 1992-2004.
  - **Mean CM effect size =.58 (28% improvement in success rate).**
  - “The strongest effect was found for contingency management interventions.”
    - **Dutra et al., *American Journal of Psychiatry*, 2008**
- Meta-analysis of 23 randomized trials of CM, with 25 or more participants in each condition, that included evaluation of post-treatment outcomes, and were published in any year through July 2020.
  - **22% greater likelihood of abstinence at a median of 24 weeks post-treatment.**
  - “These results provide support of lasting benefits of CM after reinforcers have been discontinued using objective indices of drug use outcomes.”
    - **Ginley et al., *Journal of Consulting and Clinical Psychology*, 2021**



Contents lists available at [ScienceDirect](#)

# Drug and Alcohol Dependence

journal homepage: [www.elsevier.com/locate/drugalcdep](http://www.elsevier.com/locate/drugalcdep)



Full length article

## The national implementation of Contingency Management (CM) in the Department of Veterans Affairs: Attendance at CM sessions and substance use outcomes



Dominick DePhilippis<sup>a,b,\*</sup>, Nancy M. Petry<sup>c</sup>, Marcel O. Bonn-Miller<sup>b</sup>, Sarah B. Rosenbach<sup>d</sup>, James R. McKay<sup>a,b</sup>

<sup>a</sup> Center of Excellence in Substance Addiction Treatment and Education, Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA, 19104, United States

<sup>b</sup> Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, 19104, United States

<sup>c</sup> Calhoun Cardiology Center, University of Connecticut Health Center, Farmington, CT, 06030, United States

<sup>d</sup> Steinhardt School of Culture, Education, and Human Development, New York University, New York, NY, 10003, United States

## Published Outcomes of VA's CM Implementation: 2011-2015

- **Patient Enrollment in CM**
  - From June 2011 to December 2015, VA provided CM to 2060 Veterans in 94 SUD treatment programs.
- **Attendance Outcomes**
  - Fifty percent of CM patients completed 14 or more CM sessions in a 12-week period.
  - In comparison, Oliva et al. (2013; Psychiatr. Serv.) found that only 42% of VA patients with an outpatient SUD treatment episode completed more than two sessions of care in a one year period.
- **Substance Use Outcomes**
  - 91.9% of the 27,850 Veterans' urine samples tested negative for the target substance.



# VA's Abstinence CM Implementation: Outcomes Through FY21

- 111 VA stations have made CM reinforcing abstinence available to Veterans pursuing recovery from substance use disorder.
- Over 5,700 Veterans have received Abstinence CM; and, 92% of the >73k urine samples have tested negative for the target drug(s), e.g. stimulants or cannabis!
- Regarding retention, the number of samples provided (73,656) divided by the number of Veterans who've received CM (5,711) is ~13 samples. Since CM involves twice-weekly sampling, the mean retention in treatment among CM patients is ~6.5 weeks.

# CM is Effective Across Many Patient Populations

- **Homeless:**
  - Tracy et al., 2007, *Am J Drug Alcohol Abuse*, 33(2), 253-258.
- **People with serious mental illness:**
  - Murphy et al., 2015, *DAD*, 153, 293-299.
- **Patients with PTSD:**
  - Mancino et al., *Am J Addict*, 2010; 19(2), 169-177.
- **People with HIV disease:**
  - Petry et al., 2001, *JSAT*, 21(2), 89-96.
- **Justice involved patients:**
  - DeFulio et al., 2013, *JSAT*, 45(1), 70-75.
- **Veterans:**
  - DePhilippis et al., 2018, *DAD*, 185, 367-373.
- **Patients on MOUD:**
  - Ainscough et al., 2017, *DAD*; Schottenfeld et al., 2005, *Am J Psychiatry*; Kosten et al., 2003, *DAD*.
- **Across races\*:**
  - Barry et al., 2009, *PAB*, 23(1), 168-174.
- **Across sexes:**
  - Petry and Rash, 2015, *Exp Clin Psychopharmacol*, 23(5), 369-376.
- **Pregnant women:**
  - Schottenfeld et al., 2011, *DAD*, 118(1) 48-55.
- **LGBT community:**
  - Zajac et al., 2020, *PAB*, 34(1), 128-135
  - Reback et al., 2019, *AIDS Behav*.
- **Across income levels:**
  - Rash et al., 2009, *DAD*, 104(3), 249-253.

# Why implement CM?

## For at least 7 reasons...

- 1) **It's needed and it works!**
- 2) **It can be delivered by LIPs or non-LIPs!**
- 3) **It's brief!** Sessions can be completed in as little as 6-10 minutes.
- 4) **It's low-cost!** Prize CM costs an average of \$200 in incentives per patient.
- 5) **It can be combined with any other SUD treatment, e.g. medication, psychotherapy, self-help, etc.!**
- 6) **It's endorsed by VHA policy!** “When clinically indicated, CM must be available to all patients meeting locally established patient inclusion criteria that are consistent with published evidence (VHA SUD Handbook).”
- 7) **It's fun!** Prepare for smiles, shouts, and happy dances.

**Thank you!**

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